

National Influenza Vaccination Disparities Partnership

Webinar Talking to Patients about Flu: Sharing Facts and Addressing Misconceptions and Hesitancy

January 10, 2018



Questions & Answers

Type your question into the Q&A box

Please submit your evaluation at the end of the webinar





Presenter



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Medical Director, UCSD Immunization Partnership
Member, American Academy of Pediatrics Committee on Infectious Disease

National Influenza Vaccination Disparities Partnership WEBINAR



Objectives

- Identify available flu products for the 2017-18 flu season
- Review and address common misconceptions about flu viruses and vaccine effectiveness
- Review current flu recommendation from the Advisory Committee on Immunization Practices (ACIP)
- Suggest strategies to address flu vaccine hesitancy





INFLUENZA VACCINE 2017-2018

Mark H. Sawyer MD

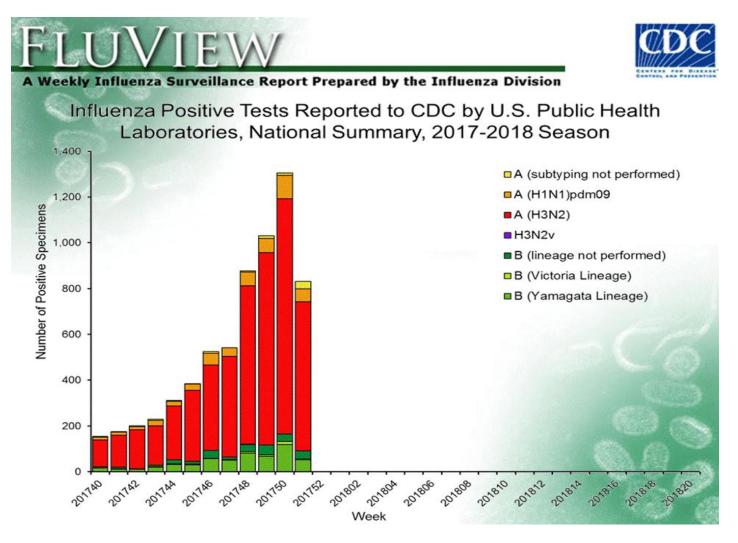
UCSD School of Medicine/Rady Children's Hospital
San Diego

San Diego Immunization Partnership



WEEKLY INFLUENZA SURVEILLANCE – POSITIVE TESTS



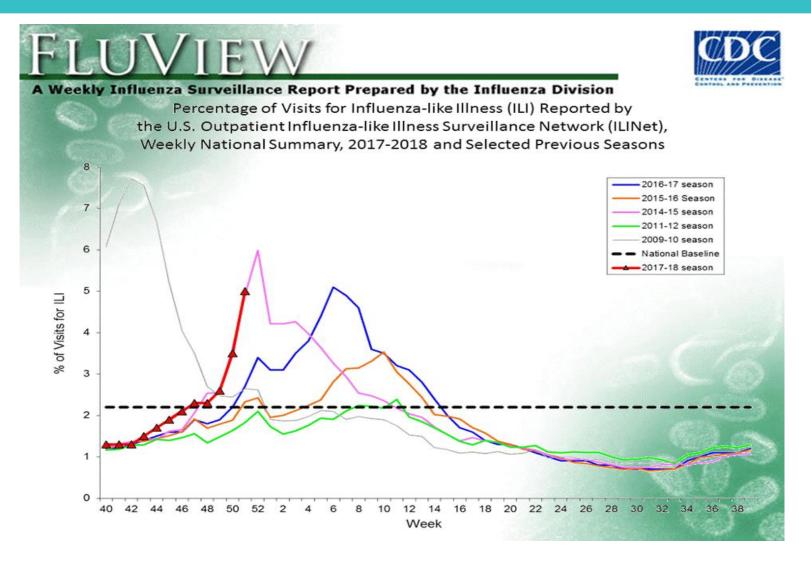


FluView: A weekly influenza surveillance report prepared by the Influenza Division under CDC.

Retrieved 1/3/18 from https://www.cdc.gov/flu/weekly/

WEEKLY INFLUENZA SURVEILLANCE – VISITS FOR ILI





FluView: A weekly influenza surveillance report prepared by the Influenza Division under CDC.

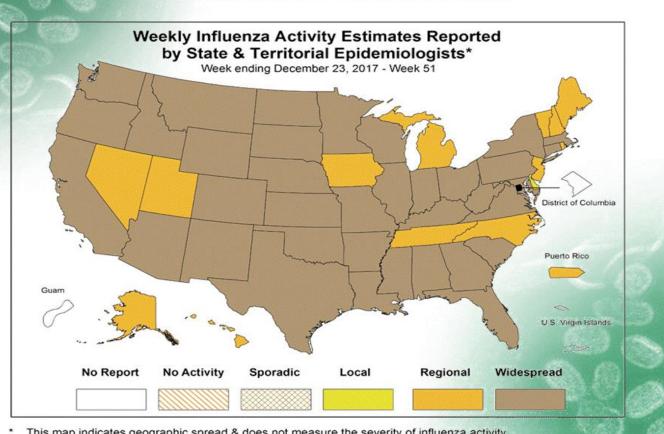
Retrieved 1/3/18 from https://www.cdc.gov/flu/weekly/

WEEKLY INFLUENZA SURVEILLANCE - ACTIVITY BY STATE & TERRITORY





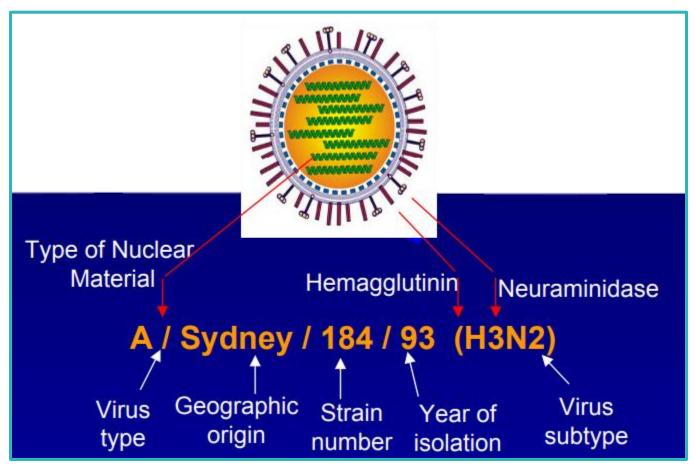
A Weekly Influenza Surveillance Report Prepared by the Influenza Division



This map indicates geographic spread & does not measure the severity of influenza activity

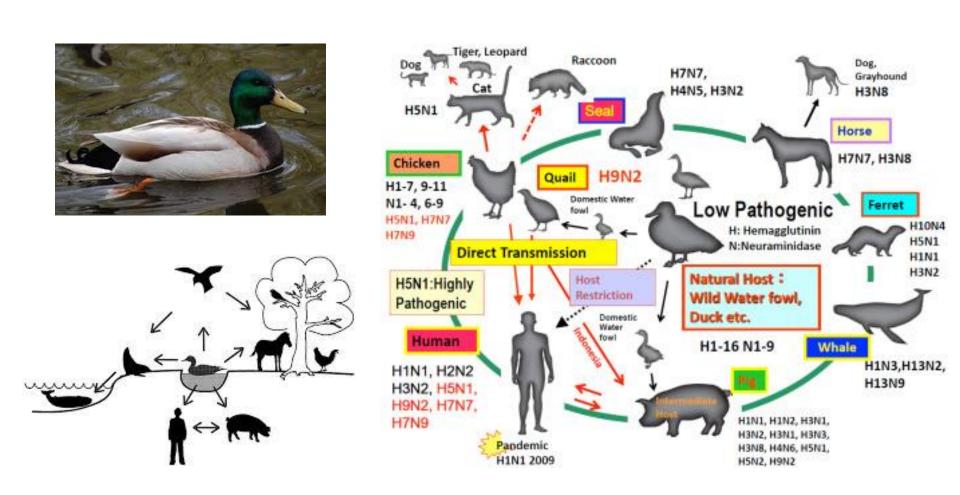
INFLUENZA VIRUS NOMENCLATURE





INFLUENZA ON EARTH





Suzuki, Y. (2013, Nov. 14). Recent research on influenza virus receptor and the mechanism of its host range mutation. Retrieved from http://www.glycoforum.gr.jp/science/glycomicrobiology/GM10/GM10E.html

HOW WE PICK INFLUENZA VACCINE STRAINS



- Worldwide surveillance
- Sophisticated laboratory analysis
 - Serologic comparisons
 - Nucleic acid sequencing
- WHO expert panel
- FDA VRBPAC-Vaccines and Related Biological Products Advisory Committee

SEASONAL INFLUENZA VACCINE PRODUCTION TIMETABLE



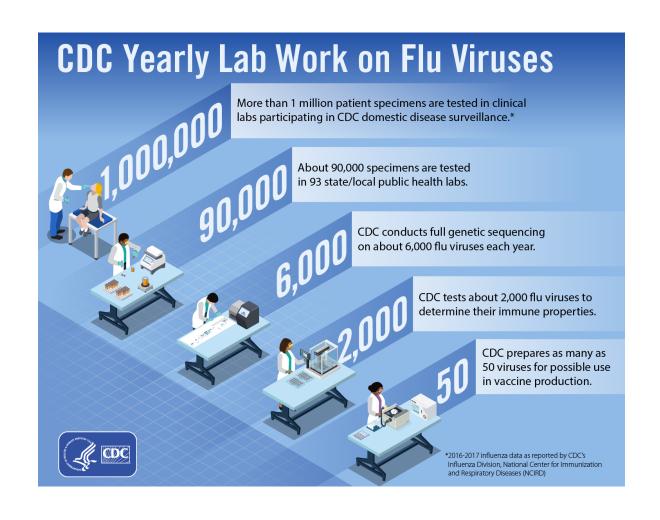
This slide, from the U.S. Food and Drug Administration, illustrates the production timeframe of seasonal influenza vaccine starting from surveillance to the administration of vaccine to the general public

Steps	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	ост	NOV	DEC
Surveillance												
Select Strains												
Reference Virus	E-											
Reagents					<u> </u>							
Production				45	ř							
Release								4 8				
Distribution								È.				
Administer												



U.S. SURVEILLANCE





WHY DO WE GET IT WRONG?



- We choose the vaccine in February
- Influenza virus is an RNA virus and subject to antigenic drift
 - For influenza virus to multiply, the RNA has to be duplicated by RNA polymerase
 - 。 RNA polymerases are not very accurate
 - RNA sequence: ...AGCUAAGAA........AGUUAAGAA...
 - Codons: ...AGC-UAA-GAAAGU-UAA-GAA...
 - Amino acids: ...XYZ........QYZ....
 - Protein:original structuredrifted structure
 - Immune response:
 good → not so good
- Primary structure

 Secondary structure

 Secondary structure

 Secondary structure

 Structure

 Quaternary structure

 Structure

 Amino acid residues

 A Helix

 Polypeptide chain

 Assembled subunits

Over time, the virus changes

2017-2018 INFLUENZA VACCINES



- Influenza A (H3N2) and Influenza B strains are unchanged
- New Influenza A (H1N1) strain A/Michigan replaces A/California based on minor changes in circulating strains
- New product licensed for infants!
 - GSK (Flulaval) licensed for children 6 months and older in November 2016

ACIP Recommendations. MMWR 2016;65:1-54/Pediatrics

2016;138(4):DOI: 10.1542/peds.2016-2527

2016-2017 INFLUENZA SEASON



US Flu VE Network: Vaccine effectiveness against influenza A/B, 2016–17

						Vaccine Ef	fectiven	tiveness		
	Influenza posi	tive	Influenza negat	ive	Un	adjusted	Ad	justed*		
Any influenza A or B virus	N vaccinated/Tota	ıl (%)	N vaccinated/Total	(%)	VE %	95% CI	VE %	95% CI		
All ages	883/2052	(43)	2761/5153	(54)	35	(27 to 41)	42	(35 to 48)		
Age group (y	r)									
6 mo-8 yr	106/353	(30)	709/1318	(54)	63	(53 to 71)	61	(49 to 70)		
9–17	123/402	(31)	245/606	(40)	35	(15 to 50)	35	(13 to 61)		
18-49	203/529	(38)	716/1629	(44)	21	(3 to 35)	19	(-1 to 34)		
50-64	203/442	(46)	537/909	(59)	41	(26 to 53)	42	(26 to 55)		
≥65	248/326	(76)	554/691	(80)	21	(-8 to 43)	25	(-5 to 46)		

^{*} Multivariate logistic regression models adjusted for site, age, sex, race/ethnicity, self-rated general health status, days from illness onset to enrollment, and calendar time of illness onset

VARIATION IN INFLUENZA VACCINE EFFECTIVENESS



Table. Adjusted vaccine effectiveness estimates for influenza seasons from 2005-2017

Influenza Season'	Reference	Study Site(s)	No. of Patients	Adjusted Overall VE (%)	95% CI
2004-05	Belongia 2009	WI	762	10	-36, 40
2005-06	Belongia 2009	WI	346	21	-52, 59
2006-07	Belongia 2009	WI	871	52	22 ,70
2007-08	Belongia 2011	WI	1914	37	22, 49
2008-09	Unpublished	WI, MI, NY, TN	6713	41	30, 50
2009-10	Griffin 2011	WI, MI, NY, TN	6757	56	23, 75
2010-11	Treanor 2011	WI, MI, NY, TN	4757	60	53, 66
2011-12	<u>Ohmit 2014</u>	WI, MI, PA, TX, WA	4771	47	36, 56
2012-13	McLean 2014	WI, MI, PA, TX, WA	6452	49	43, 55
2013-14	Gaglani 2016	WI, MI, PA, TX, WA	5999	52	44, 59
2014-15	Zimmerman 2016	WI, MI, PA, TX, WA	9311	19	10, 27
2015-16*	Jackson 2017	WI, MI, PA, TX, WA	6879	48*	41,55*
2016-17**	Unpublished final estimates	WI, MI, PA, TX, WA	7410	39**	32, 46

^{*}Estimate from Nov 2, 2015-April 15, 2016.

^{**}Interim 2016-2017 VE estimates (4/20/2016-4/9/2017) were presented to ACIP in June 2017 [743KB, 19

INFLUENZA VACCINE EFFECTIVENESS DEPENDS ON:



- How you decide if someone has influenza
- What population do you study most vaccines work less well in the very young and very old
- What do you mean by effective:
 - Prevents death
 - Prevents hospitalization
 - Prevents a visit to the doctor or emergency rom
 - Prevents any symptoms

IS THE 2017-2018 VACCINE ONLY 10% EFFECTIVE?



- Based on experience in Australia with one strain (H3N2)
- No official estimates yet for the U.S. vaccine effectiveness this season
- United States' effectiveness will depend on which strains circulate here
- So far, the majority of strains characterized in the United States are still similar to the vaccine strains

2017-2018 INFLUENZA **VACCINE PRODUCTS**



Influenza Vaccine Products for the 2017-2018 Influenza Season

Manufacturer	Trade Name	Llaw Swarfied	Mercury	A == C == ==	Vaccine Produc	t Billing Cod	le ²
Manufacturer	(vaccine abbreviation) ¹	How Supplied	Content (mcg Hg/0.5mL)	Age Group	СРТ	Medicare	
AstraZeneca	FluMist ³ (LAIV4)	0.2 mL (single-use nasal spray)	0	2 through 49 years	90672	90672	A lot of
GlaxoSmithKline	Fluarix (IIV4)	0.5 mL (single-dose syringe)	0	3 years & older	90686	90686	Alotoi
ID Biomedical Corp. of Quebec,	FluLaval (IIV4)	0.5 mL (single-dose syringe)	0	6 months & older	90686	90686	products are
a subsidiary of GlaxoSmithKline	Tideavai (iivi)	5.0 mL (multi-dose vial)	<25	6 months & older	90688	90688	•
Protein Sciences Corp.	Flublok (RIV3)	0.5 mL (single-dose vial)	0	18 years & older	90673	90673	available
Protein Sciences Corp.	Flublok (RIV4)	0.5 mL (single-dose syringe)	0	18 years & older	90682	90682	
		0.25 mL (single-dose syringe)	0	6 through 35 months	90685	90685	
	Fluzone (IIV4)	0.5 mL (single-dose syringe)	0	3 years & older	90686	90686	 Different types
		0.5 mL (single-dose vial)	0	3 years & older	90686	90686	
Sanofi Pasteur, Inc.		5.0 mL (multi-dose vial)	25	6 through 35 months	90687	90687	of vaccine
		5.0 mL (multi-dose vial)	25	3 years & older	90688	90688	
	Fluzone High-Dose (IIV3-HD)	0.5 mL (single-dose syringe)	0	65 years & older	90662	90662	
	Fluzone Intradermal (IIV4-ID)	0.1 mL (single-dose microinjection system)	0	18 through 64 years	90630	90630	Different
	Afluria (IIV3)	0.5 mL (single-dose syringe)	0	5 years & older⁴	90656	90656	
		5.0 mL (multi-dose vial)	24.5	3 years & older	90658	Q2035	presentations
	Afficia (II)/A)	0.5 mL (single-dose syringe)	0	5 years & older⁴	90686	90686	ı
Seqirus	Afluria (IIV4)	5.0 mL (multi-dose vial)	24.5	3 years & older	90688	90688	
	Fluad (aIIV3)	0.5 mL (single-dose syringe)	0	65 years & older	90653	90653	 Different ages
	Fluvirin (IIV3)	0.5 mL (single-dose syringe)	≤l	4 years & older	90656	90656	Different ages
		5.0 mL (multi-dose vial)	25	4 years & older	90658	Q2037	
	Flucelvax (ccIIV4)	0.5 mL (single-dose syringe)	0	4 years & older	90674	90674	
	riuceivax (cciiv4)	5.0 mL (multi-dose vial)	25	T years & older	90749/907565	Q2039/90756	6

FOOTNOTES

- 1. IIV3/IIV4 = egg-based trivalent/quadrivalent inactivated influenza vaccine (injectable); where necessary to refer to cell culture-based vaccine, the prefix "cc" is used (e.g., ccIIV3/ccIIV4); RIV3/RIV4 = trivalent/quadrivalent recombinant hemagglutinin influenza vaccine (injectable); aIIV3 = adjuvanted trivalent inactivated influenza vaccine.
- 2. An administration code should always be reported in addition to the vaccine product code. Note: Third party payers may have specific policies and guidelines that might require providing additional information on their claim forms.
- 3. Live attenuated influenza vaccine (LAIV4; FluMist) is not recommended by CDC's Advisory Committee on Immunization Practices for use in the U.S. for the 2017-18 influenza season.
- 4 . Affuria is approved by the Food and Drug Administration for intramuscular administration with the PharmaJet Stratis

- Needle-Free Injection System for persons age 18 through 64 years.
- 5. CPT code 90756 was released on July 1, 2017 for implementation on January 1, 2018. Payers may implement the code based on beneficiaries' needs any time after the code's release. The CPT Editorial Panel allotted a 6-month period to allow payers adequate time to prepare their systems; however, processing periods for individual payers may accommodate a more abbreviated timeframe.
- 6. The Centers for Medicare & Medicaid Services (CMS) will implement vaccine code 90756 on January 1, 2018. Before January 1, 2018, claims should use the HCPCS (Healthcare Common Procedure Coding System) Q2039 when billing Medicare.

WHAT ARE THE AGE RESTRICTIONS?



Vaccine	≥6 mos	≥3 yrs	≥4 yrs	<u>></u> 5 yrs	≥18 yrs	2-49 yrs	18-49 yrs	18-64 yrs	≥65 yrs
Fluzone/Sanofi	X								
Flulaval/GSK	X								
Fluarix/GSK		X							
Fluvirin/Novartis			X						
Flucelvax/Novartis			Х						
Afluria IIV3 and IIV4/Seqiris				X					
FluMist/MedImmune						Ø			
FluBlok/RIV 3 and 4 Protein Sciences					X				
Fluzone-Intradermal								X	
Fluzone-High dose									X
Fluad-adjuvant/Seqiris									X

INFLUENZA CHART – AGES



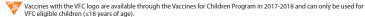




All influenza vaccines are stored in the refrigerator. Questions: Toll-free: 877-2Get-VFC (877-243-8832)

 Multi-dose vials contain preservative and cannot be given to children younger than 3 years of age and pregnant women per California law (Health and Safety Code 124172).

> Available from California Department of Public Health EZIZ.org http://eziz.org/assets/docs/IMM-859.pdf



INFLUENZA VACCINES – HOW TO KEEP THEM STRAIGHT?



- Is it trivalent or quadrivalent?
- Is it injectable or nasal?
- Is it made in eggs or in cell cultures?
- Is it a special product?
- What are its age restrictions?
- Who makes it/what is the brand name?

IS IT TRIVALENT OR QUADRIVALENT?



- Currently, there are 7 quadrivalent IIV vaccines expected for 2017-2018
- Approximately 75% of this year's vaccine will be quadrivalent
- Some companies making IIV4 vaccines will also have their old IIV3 vaccines on the market
- Some products are only available as trivalent
- CDC expresses no preference between trivalent and quadrivalent

IS IT MADE IN EGGS?



- All are made in eggs except FluBlok/Protein Sciences Corp and Flucelvax/Novartis
- Flublok is a recombinant vaccine (like Hep B vaccine) and may be referred to as RIV
- Flucelvax is a whole virus vaccine, but it is made in cells and may be referred to as
 ccIIV

IS IT A SPECIAL PRODUCT?



- IIV High dose-Fluzone High Dose/Sanofi
 - Recommended for those 65 years of age and over
 - More antigen, more local side effects
 - 。 Slightly better effectiveness in seniors
- IIV adjuvented-Fluad/Seqirus NEW this year
 - Recommended for those 65 years of age and over
- IIV Intradermal-Fluzone Intradermal/Sanofi
 - Recommended for those 18-64 years of age

WHAT HAPPENED TO LAIV?



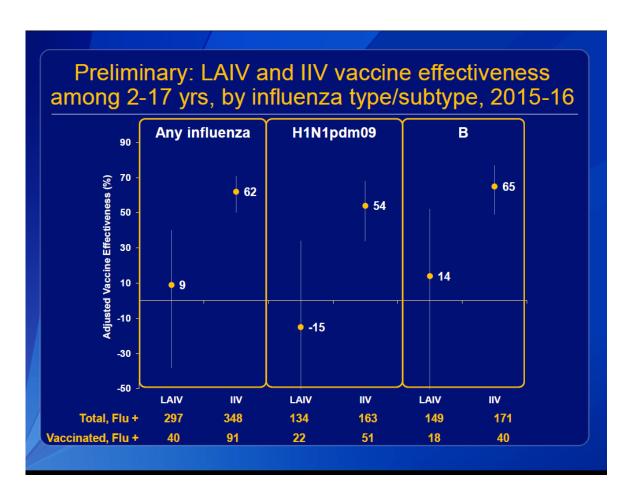




LAIV is not recommended for use this influenza season

LAIV – POOR EFFECTIVENESS

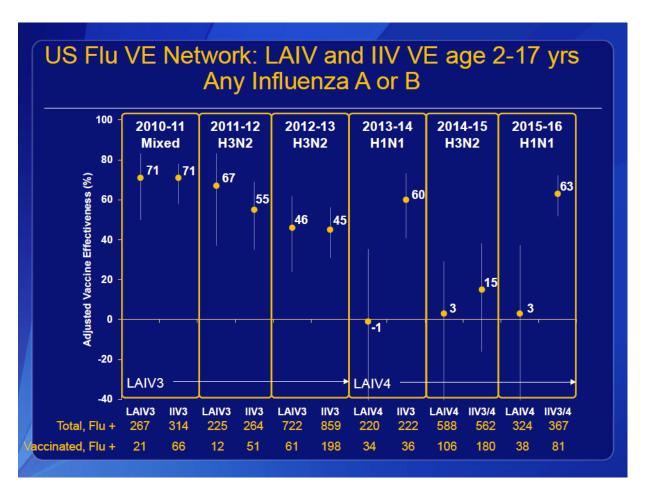




- CDC Influenza VE Network study
- Outpatients with cough illness <8 days
- Test-negative design
- PCR confirmed cases

THIS WAS NOT NEW!





Low effectiveness for 3 years in a row

https://www.cdc.gov/vaccines/acip/meetings/minutes-archive.html

ACIP RECOMMENDATION FOR 2017-2018



- The recommendation to avoid use of LAIV was originally made for the 2016–17 season
- ACIP/CDC has repeated this recommendation for 2017-2018
- This recommendation will be reevaluated as new data becomes available

WHO SHOULD GET A FLU VACCINE?





Everyone 6 months of age and older!















WHO IS NOT GETTING A FLU VACCINE?



Group	2015-2016 Unvaccinated
Seniors	37%
Adults <a>> 18 years	58%
Adults, 18-64 years, high risk	54%
Pregnant women	50% overall 33% if offered 80% if not offered
Children	41%

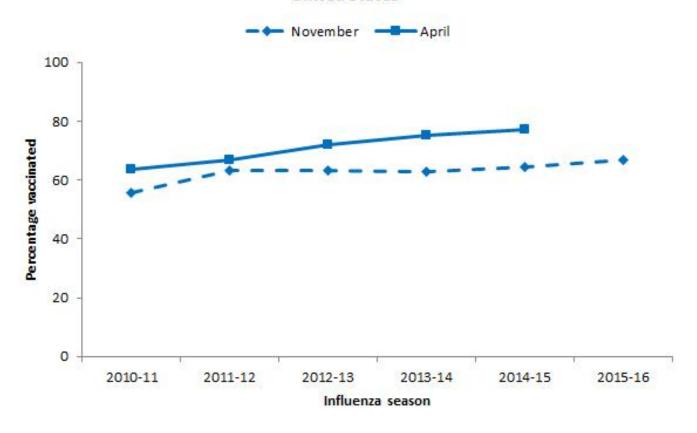
www.cdc.gov/flu

http://www.cdc.gov/flu/weekly/

HEALTHCARE WORKER INFLUENZA VACCINATION



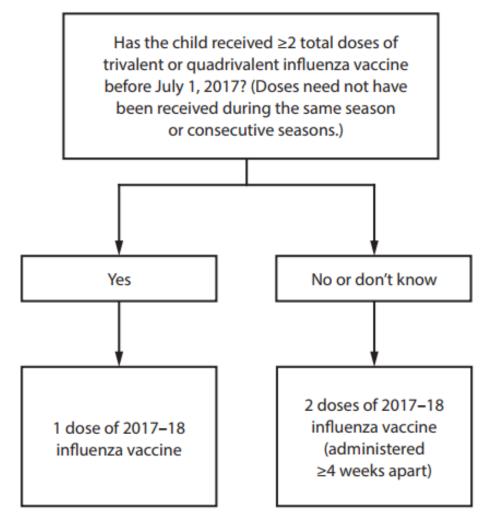
Flu vaccination coverage among health care personnel by November and April, for 2010-11, 2011-12, 2012-13, 2013-14, and 2014-15 flu seasons, and November for 2015-16 flu season, Internet panel survey, United States



TWO DOSES OF INFLUENZA VACCINE FOR YOUNG CHILDREN – UPDATE



Influenza vaccine for children aged
6 months through 8 years,
2017–18 influenza season



VACCINES DURING PREGNANCY RATIONALE



- Routine protection of adult women
- Special protection because of increased risk of disease during pregnancy (e.g., influenza)
- Protection of infants immediately after birth through passive transfer of antibody (e.g. pertussis)
- Protection of infants by prevention of transmission of disease from mother to baby

CHANGES IN PREGNANCY THAT INCREASE RISK OF INFECTION



Gestation	Risk of Hospitalization
1st trimester	7.6/10,000
2nd trimester	15.8/10,000
3rd trimester	26.2/10,000

- Modulated immune response
- Expanded vascular volume
- Decreased lung capacity
- Increased oxygen consumption

IMMUNIZATION OF PREGNANT WOMEN PROTECTS THEIR BABIES



- 316 mother-infant pairs in Bangladesh in 2004-2005
- Mothers immunized
 randomly with influenza
 vaccine or pneumococcal
 vaccine
- 63% vaccine effectiveness in preventing lab-confirmed influenza in babies
- 36% reduction in febrile respiratory in mothers

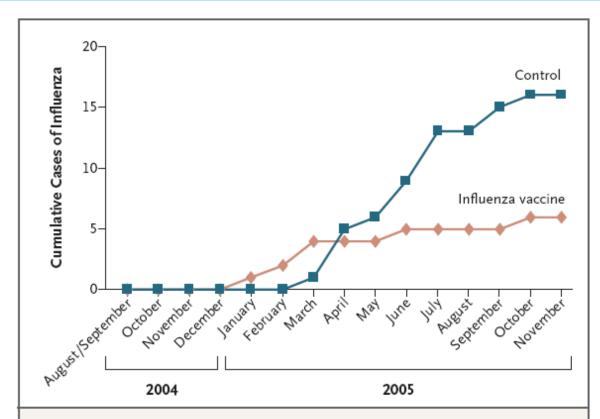


Figure 2. Cumulative Cases of Laboratory-Proven Influenza in Infants Whose Mothers Received Influenza Vaccine, as Compared with Control Subjects.

Testing for influenza antigen was performed from December 2004 to November 2005.





Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine



Association of spontaneous abortion with receipt of inactivated influenza vaccine containing H1N1pdm09 in 2010–11 and 2011–12



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Commentary

Commentary on: "Association of spontaneous abortion with receipt of inactivated influenza vaccine containing H1N1pdm09 in 2010–11 and 2011-12" ‡



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COMMENTARY



"The current findings cannot be considered causal, and could be due to chance.

Nevertheless, it is important to consider these in the context of previous work, which taken as a whole does not support any change in the ACIP recommendations to vaccinate against influenza during pregnancy. In the meantime, it is important to search for opportunities to ask the same research question in other datasets."



INFLUENZA VACCINE AND EGG ALLERGY – STOP WORRYING!



- Current manufacturing techniques have lowered the amount of ovalbumin contained in influenza vaccines to an amount that does not trigger allergic reactions
- Review of published data on 4,172 egg-allergic patients: No cases of anaphylaxis after IIV
- Anaphylaxis to influenza vaccine in egg-allergic patients is no more common than anaphylaxis to any other vaccine
- Any influenza vaccine product can be given to egg-allergic individuals, including those
 who have had anaphylaxis to egg; you should be just as prepared to treat an
 anaphylactic reaction to influenza vaccine as you are for any other vaccine
- 30-minute waiting period dropped to 15 minutes



SUMMARY



- Influenza season has started early this year
- Circulating strains of influenza are always changing
- We do not yet know how effective this year's vaccine is, but vaccination in the most important thing people can do to avoid influenza
- There is a new FDA-approved influenza vaccine product this year for 6-month-old children
- Large portions of our population do not get influenza vaccine every year; we need to keep working to improve coverage rates
- Influenza vaccine continues to be recommended routinely during pregnancy to protect the mother and the baby
- It is safe to give influenza vaccine to egg-allergic people

WHERE TO GO FOR MORE INFORMATION



- Your local health department
 (San Diego HHSA Immunization Branch [SDIZ.org])
- Your state health department
 (California Department of Public Health [www.cdph.ca.gov])
- CDC (cdc.gov/vaccines)

Questions & Answers

Type your question into the Q&A box









THANK YOU!



